

OBSTETRICS & GYNECOLOGY



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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

**The corresponding author has opted to make this information publicly available.*

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obgyn@greenjournal.org.

Date: Jul 02, 2021
To: "Moeun Son" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-1240

RE: Manuscript Number ONG-21-1240

Impact of the Coronavirus Disease 2019 (COVID-19) Pandemic on Pregnancy Outcomes in a U.S. Population

Dear Dr. Son:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Please be sure to address the Editor comments (see "EDITOR COMMENTS" below) in your point-by-point response.

Your paper will be maintained in active status for 14 days from the date of this letter. If we have not heard from you by Jul 16, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Thank you for this opportunity to review this well-written paper. This is an observational study of women delivering during pre-pandemic and pandemic. Authors found that there were no significant differences in maternal morbidities or perinatal outcomes before and after pandemic.

Abstract:

1. What maternal morbidities or perinatal outcomes were examined?
2. Was there any plan to adjust for confounders?
3. Why do you use standardized differences for some outcomes and p-values for another?
4. Did you consider the timing of testing? For example, women who had COVID-19 in the first trimester would have different impact compared to those who had COVID-19 just before delivery.
5. Did you consider symptomatic vs. asymptomatic infection?

Introduction:

1. "The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected millions worldwide, and the coronavirus disease 2019 (COVID-19) pandemic has had an enormous health burden, severely impacting healthcare delivery and utilization." Can you provide a reference?

Methods:

1. The way authors estimated prepregnancy BMI is interesting though not many patients follow recommended weight gain.
2. Why you did not limit COVID19 testing to admission testing? See the comment for Abstract #4
3. Can you comment on how you powered this study?
4. How did you adjust for confounder?
5. How did you decide those outcomes? Did you examine ICU admission, postpartum readmission etc?

Results:

1. It is unusual to combine black race and Hispanic ethnic as one group. Can you explain why you could not separately analyze?

Discussion:

1. "Our study is the first to be able to examine" Can you explain how you searched papers in what search engines?

Reviewer #2:

The authors describe the impact of the COVID-19 pandemic on pregnancy outcomes in a U.S. Population. Pre and post pandemic neonatal and maternal outcomes appear to be similar based on this large study involving over 800,000 pregnant women and 225,000 deliveries. The study compares COVID testing status cohorts, that is those that tested negative verses those that are not tested and lastly those that tested positive.

1. As pointed out, this study is unique because it has COVID testing status of most of these patients. However, the authors need to emphasize why this is an important point of this paper (and the only unique point of this paper). My interpretation is that in most studies it was not known whether the patients were tested or not, the bias being those that were tested (and hence more likely to be positive) may have been tested due to a selection bias. The patients with the greatest risk factors (which may have increased their chance of poor neonatal and maternal morbidity) for COVID were the ones more likely to be tested. Please be more specific and address this issue, this is the power of your paper.

2. Why is there such limited neonatal and maternal outcomes. Many of the outcomes associated with COVID were not considered in maternal morbidity such as, death, pulmonary complications, coagulation disorders, systemic infections. The limited birth outcomes included only that her pre term delivery and gestational weight. However, no other risk factors for preterm delivery were noted such as was its spontaneous or medically indicated or history of PTB. Would it not be possible to look at Apgars, assisted ventilation, etc in the newborn. As an EPIC hospital, I would suspect that you were able to drill down on these important outcomes

3. Although you point out that race and ethnicity appeared to be significant factor in COVID positivity. How sure are you that race is just not a marker for social economic status, access to care, educational status, etc.. Would race remain significant, if you controlled for social or vulnerability index? Some of these variables need to be adjusted. Please comment

4. You noted that you were able to determine gestational age at time of COVID testing and stated most studies looked at COVID positivity at time of delivery only. Did you note any increase in morbidity based on gestational age the patient was COVID positive? The later the COVID in gestational age the higher rate of complications? Please comment

5. The recently published prospective INTERCOVID cohort study (PMID 33885740) noted a significant increase in maternal morbidity in those patients that were COVID positive compared to those that were COVID tested negative. I think it is important to include this study in your discussion since it compares pregnant patients that did undergo COVID testing. Please comment.

6. You made a considerable number of statistical comparisons; however you made no correction for multiple measurements. In addition, a statement on how confident you are in stating that the outcomes were no different may be helpful. Please comment

7. Your discussion needs to be more focused on the uniqueness of your paper. Many papers have described increase incidence of COVID in the socially vulnerable populations, this is nothing new. More emphasis needs to be placed on how your study differs from other COVID pregnant population studies.

8. Major limitation of your study is the inability to distinguish symptomatic from asymptomatic COVID. I am confused as why this was not available in the very detailed epic records? Please comment

In addition:

Ln 79: I am confused by this statement please clarify. Furthermore, I am unsure if this is effectively explained in your discussion.

Ln222: Although your analysis of preterm birth is incomplete since your unable to document risk factors as previously

Reviewer #3:

This is an interesting and important article looking at the COVID pandemic and effects on OB outcomes.

Some questions:

Did you cluster by hospital for COVID testing (and other outcomes?)

I would imagine

- 1) Many hospitals implemented asymptomatic screening protocols at the time of admission
- 2) Hospital policy on screening, diagnosis, and treatment of maternal conditions (hypertension, etc) may have differed

and there is likely more similarities between hospital practices.

Line 1 "Analysis stratified by race and ethnicity did not show any differences in adverse birth outcomes and maternal morbidities across all three sets of comparisons (data not shown)."

- Do you mean you looked for an interaction between your COVID exposure and outcome? Or that there was no increased in maternal morbidity across the different racial/ethnic groups? That would honestly be surprising since there are disparities known in these outcomes, so I'm guessing it is the former - that should be more clear.

This sentence is also unclear:

Among those who had evidence of SARS-CoV-2 testing, Black and Hispanic women, those with public insurance, obese women, and those living within the high risk (top 25th percentile) overall SVI were more likely to test positive than test negative.

This makes it sound like they were more likely to test positive than negative which is not the case. I think you mean to say that Black and Hispanic women were more likely to test positive compared with non-Black and Hispanic women. Or you can say that women who test positive were more likely to be Black and Hispanic.

Please comment on the chi-square vs. SD statistical testing and why differences would be seen in one testing strategy but not the other.

The stillbirth outcome should be in the table so we can see the absolute numbers.

STATISTICS EDITOR COMMENTS:

Table 1: The standardized difference for proportions of maternal age > 35 yrs is incorrect. For pre vs covid, the STD = -0.186 and for the covid testing vs no testing, the STD = -0.268. Also, the differences in proportions do not appear equivalent. As pointed out by the Authors, there was significant variation in testing by census region. The missing data should be more prominently shown in the Table as a separate row labelled % missing as relevant.

Table 2: Some of the adverse events have very low frequency and there is little stats power to generalize the NS difference, (e.g., VTE/PE, Abruptio, Stillbirth.)

Tables 3 and 4 include both STD and p-values. Since some of our readers may not be familiar with STD, should follow the same format for all Tables, namely to include p-values.

General: Although it is encouraging from these data that events such as PTB were no different pre and during COVID, there is no adjustment for differences in risk profile for the two groups, that is, there is simply comparison of crude PTB etc rates. The missing data re: BMI is problematic, for example. Moreover, the PTB rates for this population were lower pre-COVID than in the entire US, so these findings may not be generalizable. The limitations section of Discussion should be longer.

EDITOR COMMENTS:

1. Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision, please remove the word "impact" from the title.
2. Please expand (1 or 2 sentences) on why standard difference scores is the appropriate analysis here, and how to interpret them, given that there will be lower familiarity with this methodology among our readership.
3. Revise the abstract to reflect the content of the manuscript. Currently the abstract seems focused on COVID positive vs COVID negative, and the primary objective of the manuscript (I believe) is pre vs during pandemic outcomes.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

- A. OPT-IN: Yes, please publish my point-by-point response letter.
- B. OPT-OUT: No, please do not publish my point-by-point response letter.

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page.

3. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

4. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), observational studies using ICD-10 data (ie, RECORD), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at <http://ong.editorialmanager.com>. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, RECORD, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

5. Your study uses ICD-10 data, please make sure you do the following:

- a. State which ICD-10-CM/PCS codes or algorithms were used as Supplemental Digital Content.
- b. Use both the diagnosis and procedure codes.
- c. Verify the selected codes apply for all years of the study.
- d. Conduct sensitivity analyses using definitions based on alternative codes.
- e. For studies incorporating both ICD-9 and ICD-10-CM/PCS codes, the Discussion section should acknowledge there may be disruptions in observed rates related to the coding transition and that coding errors could contribute to limitations of the study. The limitations section should include the implications of using data not created or collected to answer a

specific research question, including possible unmeasured confounding, misclassification bias, missing data, and changing participant eligibility over time.

f. The journal does not require that the title include the name of the database, geographic region or dates, or use of database linkage, but this data should be included in the abstract.

g. Include RECORD items 6.3 and 7.1, which relate to transparency about which codes, validation method, and linkage were used to identify participants and variables collected.

6. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions> and the gynecology data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 5,500 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

8. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

* All financial support of the study must be acknowledged.

* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.

* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.

* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."

9. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words; Reviews is 300 words; Case Reports is 125 words; Current Commentary articles is 250 words; Executive Summaries, Consensus Statements, and Guidelines are 250 words; Clinical Practice and Quality is 300 words; Procedures and Instruments is 200 words. Please provide a word count.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmgr.ovid.com/ong/accounts/abbreviations.pdf>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

12. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

13. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%).

14. Your manuscript contains a priority claim. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

15. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

16. Please review examples of our current reference style at <http://ong.editorialmanager.com> (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources"). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at <https://www.acog.org/clinical> (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document.

If the reference you are citing has been updated and replaced by a newer version, please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

17. When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should

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When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

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- * A confirmation that you have read the Instructions for Authors (<http://edmgr.ovid.com/ong/accounts/authors.pdf>), and

- * A point-by-point response to each of the received comments in this letter. Do not omit your responses to the Editorial Office or Editors' comments.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jul 16, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Torri D. Metz, MD
Associate Editor, Obstetrics

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

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Torri D. Metz, MD
Associate Editor, Obstetrics
Obstetrics & Gynecology

Dear Dr. Metz,

Thank you for the opportunity to revise our manuscript titled “The Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy Outcomes in a U.S. Population” for review and reconsideration for publication in *Obstetrics & Gynecology*. We greatly appreciate the thoughtful insights from the reviewers and have addressed their comments and questions in our responses below. We have ensured that our manuscript follows STROBE guidelines, and the checklist has been completed and uploaded.

We thank you for your consideration of our revised manuscript for publication. Please contact us if you have any questions or concerns.

Sincerely,

Moeun Son, MD, MSCI
On behalf of all co-authors



REVIEWER COMMENTS:

Reviewer #1:

Comment: Thank you for this opportunity to review this well-written paper. This is an observational study of women delivering during pre-pandemic and pandemic. Authors found that there were no significant differences in maternal morbidities or perinatal outcomes before and after pandemic.

Abstract:

1. Comment: What maternal morbidities or perinatal outcomes were examined?

Response: The aim of our study was to examine pregnancy-related morbidities rather than COVID-19 disease-related morbidities. We chose to examine pregnancy-related morbidity outcomes that have been postulated to be associated with COVID-19 given the infectious, inflammatory, and thromboembolic complications associated with SARS-CoV-2, which are listed in the Methods section. We limited perinatal outcomes to those available in the maternal medical record, namely related to gestational age at birth (for preterm birth) and birthweight.

Methods: “The pregnancy-related outcomes of interest were hypertensive disorders of pregnancy inclusive of gestational hypertension, preeclampsia, eclampsia, and hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome; placental abruption; cesarean birth; postpartum hemorrhage; and venous thromboembolism or pulmonary embolism. The birth outcomes of interest were preterm birth at less than 37 weeks of gestation; stillbirth; and birthweights small or large for gestational age.”

2. Comment: Was there any plan to adjust for confounders?

Response: Analyses of pregnancy outcomes by use of standardized differences across all three comparisons did not show significant imbalances (all standardized differences <0.1) between groups. Given non-significant findings, we did not adjust for these covariates. However, in response to reviewers, we compared pregnancy-related outcomes between women considered positive vs. negative for SARS-CoV-2 infection using chi square tests. In this context, preterm both and cesarean birth were significantly elevated in positive women. When logistic regression was performed to adjust for differences in maternal attributes, the associations between SARS-CoV-2 positivity and preterm birth and cesarean were no longer significant. We hope that these more traditional analyses give the reader more confidence in our use of standard differences as after adjustment of potential confounders, the results found with standardized differences and logistic regression were aligned.

3. Comment: Why do you use standardized differences for some outcomes and p-values for another?

Response: All differences between groups in the abstract now report only the standardized difference (SD) to improve clarity for readers. Our decision to use SDs was based on the large sample size, as SDs, unlike chi-square tests, are not influenced by sample size. The Methods section details this rationale. In the initial submission, chi-square testing and associated p-values were only shown for the positive versus negative SARS-CoV-2 infection comparison since this sample was smaller. In our revised manuscript we provide both SDs and p-values and associated rationale for SDs in this study.

Methods: “All comparisons between groups were made using standardized differences (SD). SDs compare the proportions—formulated as a series of one-vs-rest comparisons for categorical variables—in units of the pooled standard deviation (23, 24). A SD with an absolute value >0.100 indicates meaningful difference between groups (23). While chi-square tests (two-sided with p -value of 0.01) were also performed since these analyses are more familiar, SD analyses were favored for interpretation given the large sample size. With a sufficiently large sample, testing using a chi-square test is likely to demonstrate a significant p -value even when the difference in outcome between groups is negligible or meaningless (due to chance) (25, 26). SDs are not influenced by sample size and have been used to evaluate meaningful differences between groups in large cohort studies (27-29).”

4. Comment: Did you consider the timing of testing? For example, women who had COVID-19 in the first trimester would have different impact compared to those who had COVID-19 just before delivery.

Response: We were able to determine trimester at time of SARS-CoV-2 testing and have now included these data in the Results. The majority (92%) were tested during the third trimester of pregnancy, which is likely related to the 10-month study period and limited number of women who could have been tested early in their pregnancy and delivered during the study period. We have included additional analyses comparing outcomes between women who tested positive during the first two trimesters of pregnancy vs. those who tested positive during the third trimester, but we were explicit in the limitations of the sample size (n=590 in the first two trimesters vs. n=6,842 in the third trimester) and asked the readers to interpret our results with caution.

Methods: “In addition, among women who were classified as SARS-CoV-2 positive during pregnancy, we compared women who were classified as positive during the first two trimesters of pregnancy (from estimated date of conception to 28 weeks of gestation) versus those classified as positive during the third trimester of pregnancy (28 weeks of gestation and greater). Comparisons were made using SDs and chi-square tests.”

Results: “Of the 7,432 women considered positive for SARS-CoV-2 infection, the majority (n=6,842; 92%) were tested during the third trimester of pregnancy compared to the first or second trimesters (n=590, 8%). Compared to women were considered positive for SARS-CoV-2 infection during the third trimester, those who were considered positive in the first or second trimester of pregnancy were more likely to have private insurance (SD=0.122), more likely to be obese (SD=0.180), more likely to have asthma or chronic obstructive pulmonary disease (SD=0.111) or pre-gestational diabetes (SD=0.136), more likely to live in the Midwest (SD=-

0.249), and less likely to live in an urban area (SD=-0.122) (Supplement Table 1). Women considered positive for SARS-CoV-2 infection during the first or second trimester were more likely to experience preterm birth <37 weeks of gestation compared to considered positive in the third trimester of pregnancy (12.9% vs. 8.1%, SD=0.156) (Supplement Table 2)."

5. Comment: Did you consider symptomatic vs. asymptomatic infection?

Response: We appreciate the reviewer's question. Unfortunately, we were unable to distinguish symptomatic from asymptomatic SARS-CoV-2 infection. There is not standardized documentation and associated data of clinical symptoms, physical examination findings, radiographic imaging results, and associated treatments needed to make the distinction. The manuscript text has been expanded to further explain this limitation in the Discussion. Discussion: "...we could not distinguish between asymptomatic and symptomatic SARS-CoV-2 infection nor severity of disease, which has been shown to have differential effects on pregnancy outcomes (37). Given the significant variability in how these data are reported (based on symptoms, clinical exam findings, and radiographic imaging results) and captured across health systems, these data could not be consistently abstracted from Cosmos."

Introduction:

1. Comment: "The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected millions worldwide, and the coronavirus disease 2019 (COVID-19) pandemic has had an enormous health burden, severely impacting healthcare delivery and utilization." Can you provide a reference?

Response: References have been added and the sentence now reads: "The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected millions in the United States (U.S.) (1), and the coronavirus disease 2019 (COVID-19) pandemic has created an enormous health burden, severely impacting healthcare delivery and utilization (2, 3)."

Methods:

1. Comment: The way authors estimated prepregnancy BMI is interesting though not many patients follow recommended weight gain.

Response: Although patients do not always follow the Institute of Medicine (IOM) pregnancy weight-gain guidelines, this approach allowed us to reasonably estimate prepregnancy BMI for women missing these data in the EHR.

2. Comment: Why you did not limit COVID19 testing to admission testing? See the comment for Abstract #4

Response: For the comparison of women who tested positive versus negative for SARS-CoV-2, we did not limit inclusion to those tested within a specific timeframe during their pregnancy (e.g., hospital admission). We intentionally included any SARS-CoV-2 testing performed

during the span of a pregnancy. Certain outcomes (e.g., preterm birth, hypertensive disorders of pregnancy, birthweight) would have been difficult to evaluate if SARS-CoV-2 infection status was only determined at the time of delivery hospitalization given inadequate latency between exposure and outcome. However, we recognize that outpatient SARS-CoV-2 testing may have been more variable, and testing performed earlier in a pregnancy may have been more likely to have occurred in women who were symptomatic or had suspected or known exposures. This was more explicitly explained in the manuscript.

Discussion: "In addition, we were able to include any SARS-CoV-2 testing results during the span of a pregnancy. This is important because certain outcomes (e.g., preterm birth, hypertensive disorders of pregnancy, birthweight) would have been difficult to evaluate if SARS-CoV-2 infection status was only determined at the time of delivery hospitalization given inadequate latency between exposure and outcome. However, we recognize that outpatient SARS-CoV-2 testing may have been more variable and testing earlier in a pregnancy may have been more likely to be performed in women who were symptomatic or had suspected or known exposures."

3. Comment: Can you comment on how you powered this study?

Response: An a priori power calculation was not conducted for this retrospective observational study. The sample size was based on the available eligible patients in the Cosmos research platform. Nearly a million records were available for the pre- and post-pandemic comparison.

4. Comment: How did you adjust for confounder?

Response: As per our Response to Abstract Comment #2, analyses of pregnancy outcomes by use of standardized differences across all three comparisons did not show significant imbalances (all standardized differences <0.1) between groups. Given non-significant findings, we did not adjust for these covariates. However, in response to reviewers, we compared pregnancy-related outcomes between women considered positive vs. negative for SARS-CoV-2 infection using chi square tests. In this context, preterm both and cesarean birth were significantly elevated in positive women. When logistic regression was performed to adjust for differences in maternal attributes, the associations between SARS-CoV-2 positivity and preterm birth and cesarean were no longer significant. We hope that these more traditional analyses give the reader more confidence in our use of standard differences as after adjustment of potential confounders, the results found with standardized differences and logistic regression were aligned.

5. Comment: How did you decide those outcomes? Did you examine ICU admission, postpartum readmission etc?

Response: The purpose of this study was to assess pregnancy-related maternal morbidities and birth outcomes, not COVID-19 specific maternal morbidities, such as ICU admission. We chose to examine pregnancy-related morbidity outcomes that have been postulated to be associated with COVID-19 given the infectious, inflammatory, and thromboembolic complications associated with SARS-CoV-2. We plan to examine postpartum readmission in future studies.

Results:

1. Comment: It is unusual to combine black race and Hispanic ethnic as one group. Can you explain why you could not separately analyze?

Response: Thank you for this suggestion. We have separated these groups and now report race and ethnicity as non-Hispanic White, non-Hispanic Black, Hispanic, Asian, Other, and Missing separately (e.g., in Table 1)

Discussion:

1. Comment: "Our study is the first to be able to examine" Can you explain how you searched papers in what search engines?

Response: The priority claim has been removed from the manuscript.

Reviewer #2:

Comment: The authors describe the impact of the COVID-19 pandemic on pregnancy outcomes in a U.S. Population. Pre and post pandemic neonatal and maternal outcomes appear to be similar based on this large study involving over 800,000 pregnant women and 225,000 deliveries. The study compares COVID testing status cohorts, that is those that tested negative verses those that are not tested and lastly those that tested positive.

1. Comment: As pointed out, this study is unique because it has COVID testing status of most of these patients. However, the authors need to emphasize why this is an important point of this paper (and the only unique point of this paper). My interpretation is that in most studies it was not known whether the patients were tested or not, the bias being those that were tested (and hence more likely to be positive) may have been tested due to a selection bias. The patients with the greatest risk factors (which may have increased their chance of poor neonatal and maternal morbidity) for COVID were the ones more likely to be tested. Please be more specific and address this issue, this is the power of your paper.

Response: Thank you for the comment and suggestion. We agree that evidence of SARS-CoV-2 testing for nearly half of women in the COVID epoch is a unique strength of our study. As per your suggestion, this is more clearly highlighted in the Discussion.

Discussion: “In this large, diverse U.S. cohort, the frequency of adverse pregnancy-related outcomes did not meaningfully differ between those who delivered before versus during the COVID-19 pandemic. Notably, in this study, nearly half of women who delivered during the pandemic had evidence of SARS-CoV-2 testing, and there were no differences among those who were considered tested versus untested during pregnancy, nor between those who considered positive versus negative for SARS-CoV-2 infection during pregnancy.”

“Our finding that there was no meaningful difference in the frequency of preterm birth between women who delivered before compared to during the COVID-19 pandemic is consistent with much of the existing literature (4-8). However, prior studies were limited as they lacked data regarding SARS-CoV-2 testing status or only included positive SARS-CoV-2 cases when making comparisons before and during the COVID-19 pandemic. Thus, this study is a significant contribution as we have SARS-CoV-2 testing results and diagnostic codes for almost half of the women who delivered in the pandemic epoch.”

2. Comment: Why is there such limited neonatal and maternal outcomes. Many of the outcomes associated with COVID were not considered in maternal morbidity such as, death, pulmonary complications, coagulation disorders, systemic infections. The limited birth outcomes included only that her pre term delivery and gestational weight. However, no other risk factors for preterm delivery were noted such as was its spontaneous or medically indicated or history of PTB. Would it not be possible to look at Apgars, assisted ventilation, etc in the newborn. As an EPIC hospital, I would suspect that you were able to drill down on these important outcomes

Response: It is important the note that the data available in COSMOS are not the full complement of Epic variables. Participating hospital systems pass a curated (much smaller) set of variables back to Epic. In addition, the aim of our study was to examine pregnancy-related morbidities rather than COVID-19 disease-related morbidities. We chose to examine pregnancy-related morbidity outcomes that have been postulated to be associated with COVID-19 given the infectious, inflammatory, and thromboembolic complications associated with SARS-CoV-2, which are listed in the Methods section. We limited perinatal outcomes to those available in the maternal medical record, namely related to gestational age at birth (for preterm birth) and birthweight. Covariates such as Apgar score and infant mechanical ventilation are not available in the maternal record and require linkage between the maternal and infant EHRs.

Methods: “The pregnancy-related outcomes of interest were hypertensive disorders of pregnancy inclusive of gestational hypertension, preeclampsia, eclampsia, and hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome; placental abruption; cesarean birth; postpartum hemorrhage; and venous thromboembolism or pulmonary embolism. The birth outcomes of interest were preterm birth at less than 37 weeks of gestation; stillbirth; and birthweights small or large for gestational age.”

3. Comment: Although you point out that race and ethnicity appeared to be significant factor in COVID positivity. How sure are you that race is just not a marker for social economic status,

access to care, educational status, etc.? Would race remain significant, if you controlled for social or vulnerability index? Some of these variables need to be adjusted. Please comment.

Response: Thank you for this comment. We agree that race and ethnicity with respect to COVID positivity may reflect other social determinants of health. Based on your comment, we have assessed other factors available in COSMOS such as insurance type, social vulnerability index, census region, and urbanicity. The revised manuscript reflects these analysis.

Results: “Women who tested positive for SARS-CoV-2 infection were more likely to be Hispanic (21.3% vs. 15.0%, SD=0.164), less likely to be Non-Hispanic White (45.8% vs. 58.0%, SD=-0.247) or Asian (2.9% vs. 4.9%, SD=-0.105), more likely to have public insurance (30.8% vs. 22.7%, SD=0.185), more likely to be socially vulnerable (19.1% vs. 14.7%, SD=0.116), more likely to live in the South Census Region (47.3% vs. 31.0%, SD=0.338), less likely to live in the Midwest (25.1% vs. 36.5%), and more likely to be obese (35.2% vs. 29.3%, SD=0.125) compared to those testing negative (Table 3).”

4. Comment: You noted that you were able to determine gestational age at time of COVID testing and stated most studies looked at COVID positivity at time of delivery only. Did you note any increase in morbidity based on gestational age the patient was COVID positive? The later the COVID in gestational age the higher rate of complications? Please comment

Response: We were able to determine gestational age at time of SARS-CoV-2 testing and have now included these data in the Results. The majority (92%) were tested during the third trimester of pregnancy, which is likely related to the 10-month study period and limited number of women who could have been tested early in their pregnancy and delivered during the study period. We have included additional analyses comparing outcomes between women who tested positive during the first two trimesters of pregnancy vs. those who tested positive during the third trimester, but we were explicit in the limitations of the sample size (n=590 in the first two trimesters vs. n=6,842 in the third trimester) and asked the readers to interpret our results with caution.

Results: “Of the 7,432 women considered positive for SARS-CoV-2 infection, the majority (n=6,842; 92%) were tested during the third trimester of pregnancy compared to the first or second trimesters (n=590, 8%). Compared to women were considered positive for SARS-CoV-2 infection during the third trimester, those who were considered positive in the first or second trimester of pregnancy were more likely to have private insurance (SD=0.122), more likely to be obese (SD=0.180), more likely to have asthma or chronic obstructive pulmonary disease (SD=0.111) or pre-gestational diabetes (SD=0.136), more likely to live in the Midwest (SD=-0.249), and less likely to live in an urban area (SD=-0.122) (Supplement Table 1). Women considered positive for SARS-CoV-2 infection during the first or second trimester were more likely to experience preterm birth <37 weeks of gestation compared to considered positive in the third trimester of pregnancy (12.9% vs. 8.1%, SD=0.156) (Supplement Table 2).”

5. Comment: The recently published prospective INTERCOVID cohort study (PMID 33885740) noted a significant increase in maternal morbidity in those patients that were COVID positive

compared to those that were COVID tested negative. I think it is important to include this study in your discussion since it compares pregnant patients that did undergo COVID testing. Please comment.

Response: Thank you for this suggestion. We have added the results of the INTERCOVID cohort study to the Discussion section of our manuscript.

Discussion: “Similarly, the INTERCOVID multinational cohort study (36) found that women with a COVID-19 diagnosis were at higher risk for preeclampsia and eclampsia, severe infections, intensive care unit admission, maternal mortality, preterm birth, medically indicated preterm birth, severe neonatal morbidity index, and severe perinatal morbidity and mortality index compared to unmatched, consecutive women without a COVID-19 diagnosis. In this study, women were considered positive for COVID-19 based upon multiple criteria (varying laboratory tests, radiologic findings, or pre-defined symptoms) while those considered not to have COVID-19 were simply women who did not meet the aforementioned criteria, not those who were known to be tested and tested negative.”

6. Comment: You made a considerable number of statistical comparisons; however, you made no correction for multiple measurements. In addition, a statement on how confident you are in stating that the outcomes were no different may be helpful. Please comment

Response: All analyses were performed using standardized differences, which are measures of effect size and not hypothesis tests. For the chi-square comparisons, the p-values were so small that even conservative adjustment, such as with a Bonferroni correction, would not have altered conclusions. Given the relatively smaller sample size for the cohort of women tested for SARS-CoV-2, for which we also included traditional hypothesis testing, the only significant p-values (at alpha = 0.05) for the positive vs. negative comparison were for preterm birth (p=0.007) and cesarean birth (p=0.002). We have included post-hoc analyses, adjusting for significant baseline characteristics (maternal age, maternal race and ethnicity, insurance type, high-risk SVI, obesity, chronic hypertension, pre-gestational diabetes, heart disease, and urban zip code) to further investigate the effect of the COVID-19 epoch on these particular outcomes. After adjustment, we found no difference between the two epochs and adjustment for multiple comparisons is not necessary.

Methods: “Two post-hoc mixed effects logistic regression models were used to further examine the association between women with and without evidence of SARS-CoV-2 test positivity during pregnancy and the risk for preterm birth at less than 37 weeks of gestation and cesarean birth. The model was adjusted for relevant baseline characteristics (p<0.01) and included hospital system as a random intercept. Although the SD did not support a meaningful difference (SD <0.100) in risk of preterm birth or cesarean birth frequency between women with and without evidence of SARS-CoV-2 infection, this analysis was performed because of the significant p-values (p<0.01) observed in the context of the smaller cohort of pregnant women with evidence of SARS-CoV-2 testing and anticipated interest among the obstetrics community.”

7. Comment: Your discussion needs to be more focused on the uniqueness of your paper. Many papers have described increase incidence of COVID in the socially vulnerable populations, this is nothing new. More emphasis needs to be placed on how your study differs from other COVID pregnant population studies.

Response: Thank you for this comment and suggestion. We have revised the Discussion (excerpts below) to emphasize the unique strengths of our study compared to the existing literature, namely our large diverse sample, SARS-COV-2 testing results for nearly half of the women in the pandemic epoch, and our ability to make comparisons before and during the COVID pandemic and within the COVID pandemic epoch itself.

Discussion: “In this large, diverse U.S. cohort, the frequency of adverse pregnancy-related outcomes did not meaningfully differ between those who delivered before versus during the COVID-19 pandemic. Notably, in this study, nearly half of women who delivered during the pandemic had evidence of SARS-CoV-2 testing, and there were no differences among those who were considered tested versus untested during pregnancy, nor between those who considered positive versus negative for SARS-CoV-2 infection during pregnancy.”

“Our finding that there was no meaningful difference in the frequency of preterm birth between women who delivered before compared to during the COVID-19 pandemic is consistent with much of the existing literature (4-8). However, prior studies were limited as they lacked data regarding SARS-CoV-2 testing status or only included positive SARS-CoV-2 cases when making comparisons before and during the COVID-19 pandemic. Thus, this study is a significant contribution as we have SARS-CoV-2 testing results and diagnostic codes for almost half of the women who delivered in the pandemic epoch.”

“Strengths of this study include the large number of pregnant women and diversity of U.S. hospitals included in the analytic cohort. The size of our cohort enabled us to examine pregnant women who delivered before and during the COVID-19 pandemic as well as SARS-CoV-2 testing status of all individuals included in the pandemic epoch, and almost half were considered negative or positive for SARS-CoV-2 infection. This is unique to our study as prior studies have been limited by use of only the presence or absence of diagnosis codes for COVID-19 infection (14, 36), or small numbers of confirmed tested women. Additionally, our data were obtained from 465 hospitals across all four Census-Bureau regions of the U.S. This is an important strength since SARS-CoV-2 infection cases have fluctuated significantly over time with migratory geographical hot-spots.”

8. Comment: Major limitation of your study is the inability to distinguish symptomatic from asymptomatic COVID. I am confused as why this was not available in the very detailed epic records? Please comment

Response: Although EHR records can be very detailed, there is not standardized documentation and associated data of clinical symptoms, physical examination findings, radiographic imaging results, and associated treatments needed to make the distinction. Each health system’s EHR is individually customized, and therefore there is significant variability across health systems in how these data are captured. The manuscript text has been expanded to further explain this limitation in the Discussion.

Discussion: "...we could not distinguish between asymptomatic and symptomatic SARS-CoV-2 infection nor severity of disease, which has been shown to have differential effects on pregnancy outcomes (37). Given the significant variability in how these data are reported (based on symptoms, clinical exam findings, and radiographic imaging results) and captured across health systems, these data could not be consistently abstracted from Cosmos."

In addition:

Comment: Ln 79: I am confused by this statement please clarify. Furthermore, I am unsure if this is effectively explained in your discussion.

Comment: Ln222: Although your analysis of preterm birth is incomplete since your unable to document risk factors as previously

Response: To address the reviewer's concern and anticipated interest among readers, we used a post-hoc mixed effects logistic regression model to further examine the association between SARS-CoV-2 test positivity during pregnancy and the risk for preterm birth at less than 37 weeks of gestation and cesarean birth. This is now described in the manuscript.

Methods: "Two post-hoc mixed effects logistic regression models were used to further examine the association between women with and without evidence of SARS-CoV-2 test positivity during pregnancy and the risk for preterm birth at less than 37 weeks of gestation and cesarean birth. The model was adjusted for relevant baseline characteristics ($p < 0.01$) and included hospital system as a random intercept. Although the SD did not support a meaningful difference ($SD < 0.100$) in risk of preterm birth or cesarean birth frequency between women with and without evidence of SARS-CoV-2 infection, this analysis was performed because of the significant p-values ($p < 0.01$) observed in the context of the smaller cohort of pregnant women with evidence of SARS-CoV-2 testing and anticipated interest among the obstetrics community."

Reviewer #3:

This is an interesting and important article looking at the COVID pandemic and effects on OB outcomes.

Some questions:

Comment: Did you cluster by hospital for COVID testing (and other outcomes?)

I would imagine

- 1) Many hospitals implemented asymptomatic screening protocols at the time of admission
- 2) Hospital policy on screening, diagnosis, and treatment of maternal conditions (hypertension, etc) may have differed and there is likely more similarities between hospital practices.

Response: We agree with the reviewer that there are likely variations across hospitals with regard to COVID-19 screening and SARS-CoV-2 testing protocols. In addition, there are likely variations across hospitals with regard to the identification and management of pregnancy-

related morbidities. Unfortunately, were unable to assess hospital level policies. To maintain anonymity of the data, hospital level characteristics are not compared in Cosmos.

Comment: Line 1 "Analysis stratified by race and ethnicity did not show any differences in adverse birth outcomes and maternal morbidities across all three sets of comparisons (data not shown)." Do you mean you looked for an interaction between your COVID exposure and outcome ? Or that there was no increased in maternal morbidity across the different racial/ethnic groups? That would honestly be surprising since there are disparities known in these outcomes, so I'm guessing it is the former - that should be more clear.

Response: Thank you for highlighting this confusing wording. The sentence now reads:
Results: "Analyses stratified by race/ethnicity, high-risk SVI, and public insurance type did not show evidence of effect modification in adverse pregnancy-related outcomes across all three sets of comparisons (data not shown)."

Comment: This sentence is also unclear: Among those who had evidence of SARS-CoV-2 testing, Black and Hispanic women, those with public insurance, obese women, and those living within the high risk (top 25th percentile) overall SVI were more likely to test positive than test negative. This makes it sound like they were more likely to test positive than negative which is not the case. I think you mean to say that Black and Hispanic women were more likely to test positive compared with non-Black and Hispanic women. Or you can say that women who test positive were more likely to be Black and Hispanic.

Response: Thank you for highlighting this incorrect wording. This sentence now reads:
"Women who tested positive for SARS-CoV-2 infection were more likely to be Hispanic (21.3% vs. 15.0%, SD=0.164), less likely to be Non-Hispanic White (45.8% vs. 58.0%, SD=-0.247) or Asian (2.9% vs. 4.9%, SD=-0.105), more likely to have public insurance (30.8% vs. 22.7%, SD=0.185), more likely to be socially vulnerable (19.1% vs. 14.7%, SD=0.116), more likely to live in the South Census Region (47.3% vs. 31.0%, SD=0.338), less likely to live in the Midwest (25.1% vs. 36.5%), and more likely to be obese (35.2% vs. 29.3%, SD=0.125) compared to those testing negative (Table 3)."

Comment: Please comment on the chi-square vs. SD statistical testing and why differences would be seen in one testing strategy but not the other.

Response: We have added this information and our rationale for favoring SDs to the Methods section.

Methods: "All comparisons between groups were made using standardized differences (SD). SDs compare the proportions—formulated as a series of one-vs-rest comparisons for categorical variables—in units of the pooled standard deviation (23, 24). A SD with an absolute value >0.100 indicates meaningful difference between groups (23). While chi-square tests (two-sided with p -value of 0.01) were also performed since these analyses are more familiar, SD

analyses were favored for interpretation given the large sample size. With a sufficiently large sample, testing using a chi-square test is likely to demonstrate a significant p -value even when the difference in outcome between groups is negligible or meaningless (due to chance) (25, 26). SDs are not influenced by sample size and have been used to evaluate meaningful differences between groups in large cohort studies (27-29).”

Comment: The stillbirth outcome should be in the table so we can see the absolute numbers.

Response: Thank you pointing out this unintentional omission. The stillbirth outcome has been added to Table 4.

STATISTICS EDITOR COMMENTS:

Comment: Table 1: The standardized difference for proportions of maternal age > 35 yrs is incorrect. For pre vs covid, the STD = -0.186 and for the covid testing vs no testing, the STD = -0.268. Also, the differences in proportions do not appear equivalent. As pointed out by the Authors, there was significant variation in testing by census region. The missing data should be more prominently shown in the Table as a separate row labelled % missing as relevant.

Response: Thank you for highlighting these errors. We have corrected them and, as the Statistics Editor suggested, have separate rows for % missing in the Tables for variables with notable missing data.

Comment: Table 2: Some of the adverse events have very low frequency and there is little stats power to generalize the NS difference, (e.g., VTE/PE, Abruptio, Stillbirth.)

Response: We agree that some of the outcomes examined are still rare occurrences and we were likely underpowered to adequately assess these outcomes despite the size of our cohort. This limitation has been added to the Discussion.

Discussion: “...some of the outcomes examined are rare occurrences (e.g., venous thromboembolism, pulmonary embolism, and stillbirth), and we were likely underpowered to adequately assess these outcomes despite our very large sample size.”

Comment: Tables 3 and 4 include both STD and p -values. Since some of our readers may not be familiar with STD, should follow the same format for all Tables, namely to include p -values.

Response: All tables now include both standardized differences and p -values.

Comment: General: Although it is encouraging from these data that events such as PTB were no different pre and during COVID, there is no adjustment for differences in risk profile for the two

groups, that is, there is simply comparison of crude PTB etc rates. The missing data re: BMI is problematic, for example. Moreover, the PTB rates for this population were lower pre-COVID than in the entire US, so these findings may not be generalizable. The limitations section of Discussion should be longer.

Response: Only singleton births were included in this analysis; therefore, the overall preterm birth (PTB) rate for this population (7.7% in the pre-COVID epoch and 7.6% in the COVID epoch) is not dissimilar to published U.S. data in which the 2019 PTB (less than 37 weeks of gestation) rate nationally was 8.4% (Martin JA et. al, National Vital Statistics Report, Volume 70, Number 2, 2021).

EDITOR COMMENTS:

1. Comment: Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision, please remove the word "impact" from the title.

Response: The word "impact" has been removed from the title. The title is now: "The Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy Outcomes in a U.S. Population"

2. Comment: Please expand (1 or 2 sentences) on why standard difference scores is the appropriate analysis here, and how to interpret them, given that there will be lower familiarity with this methodology among our readership.

Response: The explanation of the use of standardized differences has been expanded in the Methods section.

Methods: "All comparisons between groups were made using standardized differences (SD). SDs compare the proportions—formulated as a series of one-vs-rest comparisons for categorical variables—in units of the pooled standard deviation (23, 24). A SD with an absolute value >0.100 indicates meaningful difference between groups (23). While chi-square tests (two-sided with p -value of 0.01) were also performed since these analyses are more familiar, SD analyses were favored for interpretation given the large sample size. With a sufficiently large sample, testing using a chi-square test is likely to demonstrate a significant p -value even when the difference in outcome between groups is negligible or meaningless (due to chance) (25, 26). SDs are not influenced by sample size and have been used to evaluate meaningful differences between groups in large cohort studies (27-29)."

3. Comment: Revise the abstract to reflect the content of the manuscript. Currently the abstract seems focused on COVID positive vs COVID negative, and the primary objective of the manuscript (I believe) is pre vs during pandemic outcomes.

Response: Thank you for this suggestion. We have revised the abstract and manuscript accordingly.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

A. OPT-IN: Yes, please publish my point-by-point response letter.

B. OPT-OUT: No, please do not publish my point-by-point response letter.

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA), which must be completed by all authors. When you uploaded your manuscript, each co-author received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please check with your coauthors to confirm that they received and completed this form, and that the disclosures listed in their eCTA are included on the manuscript's title page.

Response: It has been confirmed that my coauthors and I have or will complete this form, and do not have any disclosures to report. Please note that one co-author will be rescinding her co-authorship, and she has notified the Editorial Office.

3. For studies that report on the topic of race or include it as a variable, authors must provide an explanation in the manuscript of who classified individuals' race, ethnicity, or both, the classifications used, and whether the options were defined by the investigator or the participant. In addition, the reasons that race/ethnicity were assessed in the study also should be described (eg, in the Methods section and/or in table footnotes). Race/ethnicity must have been collected in a formal or validated way. If it was not, it should be omitted. Authors must enumerate all missing data regarding race and ethnicity as in some cases, missing data may comprise a high enough proportion that it compromises statistical precision and bias of analyses by race.

Use "Black" and "White" (capitalized) when used to refer to racial categories. The nonspecific category of "Other" is a convenience grouping/label that should be avoided, unless it was a prespecified formal category in a database or research instrument. If you use "Other" in your study, please add detail to the manuscript to describe which patients were included in that category.

Response: Race and ethnicity is included as a baseline variable characteristic, in addition to other demographic variables, to provide descriptive information to the readers about our cohort demographics and highlight the diversity of our included patient population. All table footnotes have been revised to provide more clarity about this variable.

4. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), observational studies using ICD-10 data (ie, RECORD), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at <https://nam12.safelinks.protection.outlook.com/?url=http%3A%2F%2Fong.editorialmanager.com%2F&data=04%7C01%7Cmoeun.son%40yale.edu%7Ceabacf86c8af42e6a52d08d93d715d31%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C1%7C637608379382050920%7CUnknwn%7CTWFpbGZsb3d8eyJWljoimC4wLjAwMDAiLCJQJjoiV2luMzliLCJBTil6lk1haWwiLCJXVCI6Mn0%3D%7C1000&data=xU4FNzmKhzRD4bm%2BCTCdGK%2BEFX1MjTY06jDV7ihCUs%3D&reserved=0>. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, RECORD, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

Response: We have ensured that our manuscript follows STROBE guidelines, and the checklist has been completed.

5. Your study uses ICD-10 data, please make sure you do the following:

- a. State which ICD-10-CM/PCS codes or algorithms were used as Supplemental Digital Content.
- b. Use both the diagnosis and procedure codes.
- c. Verify the selected codes apply for all years of the study.
- d. Conduct sensitivity analyses using definitions based on alternative codes.
- e. For studies incorporating both ICD-9 and ICD-10-CM/PCS codes, the Discussion section should acknowledge there may be disruptions in observed rates related to the coding transition and that coding errors could contribute to limitations of the study. The limitations section should include the implications of using data not created or collected to answer a specific research question, including possible unmeasured confounding, misclassification bias, missing data, and changing participant eligibility over time.
- f. The journal does not require that the title include the name of the database, geographic region or dates, or use of database linkage, but this data should be included in the abstract.
- g. Include RECORD items 6.3 and 7.1, which relate to transparency about which codes, validation method, and linkage were used to identify participants and variables collected.

Response: ICD-10-CM codes were used for this data and specific codes used are included in the Supplement. The selected codes apply for all years of the study.

6. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions

at <https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fpractice-management%2Fhealth-it-and-clinical-informatics%2Frevitalize-obstetrics-data-definitions&data=04%7C01%7Cmoeun.son%40yale.edu%7Ceabacf86c8af42e6a52d08d93d715d31%7Cdd8cbabb21394df8b4114e3e87abeb5c%7C0%7C1%7C637608379382050920%7CUnkn0wn%7CTWFpbGZsb3d8eyJWljiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C1000&odata=6M9VyY7N7mYFBgt8b0k2b0QQ2YnUAILQUha71SxBBjQ%3D&reserved=0> and the gynecology data definitions

at <https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fpractice-management%2Fhealth-it-and-clinical-informatics%2Frevitalize-gynecology-data-definitions&data=04%7C01%7Cmoeun.son%40yale.edu%7Ceabacf86c8af42e6a52d08d93d715d31%7Cdd8cbabb21394df8b4114e3e87abeb5c%7C0%7C1%7C637608379382050920%7CUnkn0wn%7CTWFpbGZsb3d8eyJWljiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C1000&odata=4MeCYyOpefHbGB%2B36Xs45bwy1jGo%2B5DRr%2F1GNDUcBZi%3D&reserved=0>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Response: Only standard abbreviations have been used in the manuscript.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 5,500 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

Response: This original research manuscript does not exceed the word limit.

8. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

- * All financial support of the study must be acknowledged.
- * Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
- * All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.

* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."

Response: The following guidelines have been reviewed and are not applicable to this manuscript. There was no financial support, no manuscript preparation assistance, no acknowledgements, or presentations at any meetings.

9. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limit for Original Research articles is 300 words; Reviews is 300 words; Case Reports is 125 words; Current Commentary articles is 250 words; Executive Summaries, Consensus Statements, and Guidelines are 250 words; Clinical Practice and Quality is 300 words; Procedures and Instruments is 200 words. Please provide a word count.

Response: We have reviewed the abstract and believe it is consistent with the manuscript. The abstract length is within the recommendation, and a word count has been provided.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at <https://nam12.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Fabbreviations.pdf&data=04%7C01%7Cmoeun.son%40yale.edu%7Ceabacf86c8af42e6a52d08d93d715d31%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C1%7C637608379382050920%7CUnknown%7CTWFpbGZsb3d8eyJWljoiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTil6Ik1haWwiLCJXVCi6Mn0%3D%7C1000&data=TN8wEXERNIN%2F14giHA%2BWnJAKDsulJF3AB3JPf2qcDLg%3D&reserved=0>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

Response: The virgule symbol is only used to express measurements in the manuscript.

12. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

Response: The term “insurance provider” has been changed to “insurance carrier.”

13. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Response: Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%).

Standardized differences were used for statistical comparisons. Per the request of the reviewers, p-values were also added to all tables. The presentation of data is now standardized throughout the manuscript.

14. Your manuscript contains a priority claim. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

Response: The priority claim has been removed from the manuscript.

15. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online

here: https://nam12.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Ftable_checklist.pdf&data=04%7C01%7Cmoeun.son%40yale.edu%7Ceabacf86c8af42e6a52d08d93d715d31%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C1%7C637608379382050920%7CUnknown%7CTWFpbGZsb3d8eyJWljoimC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6Ikl1haWwiLCJXVCI6Mn0%3D%7C1000&data=ChNGfbqHrxXcmxKBXk6xqOmL12ft22Ssvq7XmWPNKDo%3D&reserved=0.

Response: The tables have been edited to adhere to the journal’s Table Checklist.

16. Please review examples of our current reference style

at <https://nam12.safelinks.protection.outlook.com/?url=http%3A%2F%2Fong.editorialmanager.com%2F&data=04%7C01%7Cmoeun.son%40yale.edu%7Ceabacf86c8af42e6a52d08d93d715d31%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C1%7C637608379382060916%7CU>

[known%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C1000&reserved=0](https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fclinical&data=04%7C01%7Cmoeun.son%40yale.edu%7Ceabacf86c8af42e6a52d08d93d715d31%7Cdd8cbabb21394df8b4114e3e87abeb5c%7C0%7C1%7C637608379382060916%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C1000&reserved=0) (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources"). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

Response: The references have been formatted to the Obstetrics and Gynecology style.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at <https://nam12.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.acog.org%2Fclinical&data=04%7C01%7Cmoeun.son%40yale.edu%7Ceabacf86c8af42e6a52d08d93d715d31%7Cdd8cbabb21394df8b4114e3e87abeb5c%7C0%7C1%7C637608379382060916%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzliLCJBTiI6IjEhaWwiLCJXVCi6Mn0%3D%7C1000&reserved=0> (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document.

If the reference you are citing has been updated and replaced by a newer version, please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

Response: ACOG documents are not cited in this manuscript.

17. When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

Response: The figure which was created in Microsoft Word has been submitted as a separate file.